

PATENT ABSTRACTS OF JAPAN

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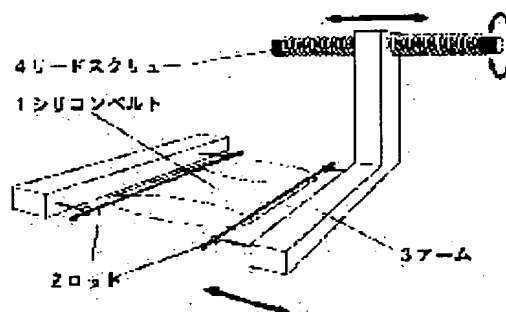
(71)Applicant : TAKEMASA TORU

(22)Date of filing : 02.12.1996

(72)Inventor : TAKEMASA TORU
ICHIKAWA MASAO**(54) LOADING DEVICE OF EXPANDING AND CONTRACTING STIMULATION FOR CULTURING CELL BY USING SILICONE BELT****(57)Abstract:**

PROBLEM TO BE SOLVED: To obtain the subject device capable of setting an expanding and contracting stimulation or extending stimulation imparted to culturing cells in high accuracy by using a belt-like silicone membrane as a carrier.

SOLUTION: The subject device is constituted by using a silicone membrane formed into a belt-like shape as a carrier 1 and expanded and contracted by a high torque stepping motor and a lead screw 4. Two rods 2 are inserted in the interior of the silicone belt having cells, etc., added thereto, and are hung on right and left arms 3 respectively. An extending rate is set in a high accuracy within a range of 0% to at least 110% at 0.1% interval, and a change of a expanding and contracting acceleration, extending time, a moment stop, a frequency of the expansion and contraction, etc., is readily performed without changing a hard wear.

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CLAIMS

[Claim(s)]

[Claim 1] Flexible stimulus load equipment for cultured cells using the belt-like silicon film (1) to support [claim 2] Flexible stimulus load equipment for cultured cells according to claim 1 which used the stepping motor for power and changed the rotation into rectilinear motion by the leading screw (4) [claim 3] Flexible stimulus load equipment for cultured cells according to claim 1 which used the stepping motor for power and changed the rotation into rectilinear motion by the timing belt.

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the technique of giving a cultured cell and an organization a flexible stimulus and an expansion stimulus.

[0002]

[Description of the Prior Art] Generally a cell is cultivated on the silicon film which coated the extra-cellular matrix etc. for giving a flexible stimulus to a cultured cell etc., and the method of making it expand and contract the whole silicon film is taken. As equipment which extends the silicon film conventionally, it thought from the directivity of expansion and, on the other hand, the thing [drawing 4] of tropism and the thing [drawing 5] of a radial have been used.

[0003] On the other hand, the approach [the conventional approach 1] of extending according to the device in which rotation of the synchronous motor using [fix and] a cam (12) for it to which the thing of tropism attaches the both ends of the rectangular silicon film (9) using a clip (11) is changed into a piston action, returning to (10) and the original die length, or carrying out (9) is used [drawing 4].

[0004] The approach [the conventional approach 2] of extending the silicon film of a bottom because the thing of a radial attracts from the bottom the petri dish (15) whose base (13) is made of the silicon film, or returning to the condition of (14) origin, or carrying out (13) is used [drawing 5]. (U.S. flex-time cel company: patent numbers 4789601, 4822741, and 4839280)

[0005]

[Problem(s) to be Solved by the Invention]

The [conventional approach 1] The expansion direction was made hard to analyze, since the strain of the shape of a spool as [when it extends,] shown in (10), since [attaching by the ability clip (11) doing] it is fixed is produced so that it may not separate, even if it extends the both ends of the silicon film (9), and the condition of deformation changes with locations. And although sterilization actuation was required for the equipments containing adjustment catches, such as a clip, there were few the springs and screws of the quality of the material which are equal to the autoclave sterilization of a repeat elevated temperature, high pressure, and high humidity etc., and are easy to do processing etc., and the fixed actuation at every experiment was still more complicated. Moreover, the synchronous motor and the device using a cam were troublesome in order that modification of the amplitude might also rearrange the hardware itself, and a setup of [flexible movement which includes a halt periodically], and modification of flexible acceleration were impossible.

[0006] The [conventional approach 2] The expansion direction was made hard for the tension direction to change with locations and to analyze, since tension is applied to the extended silicon film (14) at a radial. Moreover, it was also pointed out only by the periphery of the silicon film being extended that most center sections are not

extended. Furthermore also in the periphery, the rate of expansion also had the limit of being structurally obtained only to 24%. And since silicon was extended by the indirect approach of suction, compared with the set-up rate of expansion, deviation may have appeared in the actual rate of expansion by wear of packing, adhesion of dust, etc. Moreover, since magnitude was decided, the ready-made silicon petri dish had few degrees of freedom, and they were expensive. The suction unit (a ** computer, suction pump) was also still more nearly large-scale, and it takes a location and was expensive.

[0007]

[Means for Solving the Problem] In order that this invention may solve such a technical problem, it is made to expand and contract using a high torque stepping motor and a leading screw using what made the silicon film of support the shape of a belt (1) [drawing 1 R> 1]. Two rods (2) are inserted inside the silicon belt (1) to which the cell etc. has adhered, and the rod is hooked on an arm (3) on either side, respectively. Rotation of the clockwise rotation and counterclockwise rotation of a high torque stepping motor is changed into the piston action of an arm using a leading screw (4). A silicon belt can be made to expand and contract by shaking an arm at right and left.

[0008]

[Example] Using sill pot 184 W/C of Dow Corning Asia, a silicon belt makes a template the test tube or silicon rod of glass, makes a coat from a dipping method, and makes it harden applying heat. A silicon belt will be made if the stripped-off saccate silicon is cut into round slices.

[0009] Although autoclave sterilization, a rod, and an arm perform dry sterilization independently, respectively in a silicon belt, it is also easy to assemble in sterile.

[0010] Rotation of a high torque stepping motor was changed into rectilinear motion using Kirk's leading screw.

[0011] Rotation of a high torque stepping motor can also be changed into rectilinear motion using a timing belt.

[0012] The motion of the stepping motor of JAPAN SERVO CO., LTD. was controlling using the intelligent control driver of the company, a setup of the rate of expansion was attained in a high precision of a unit 0.1% in 0 to at least 110% of range, and it has been set up easily, without modification of a program including conversion of flexible acceleration, expansion time amount and halt / flexible frequency etc. also rearranging hardware [finishing / sterilization].

[0013] It is more convenient to make desorption possible using a screw etc. from a part for the moving part connected with a leading screw, since the part which hooks the rod of an arm has the need for sterilization.

[0014] If latex rubber is used instead of latex silicon when there is no need for microscope observation, it is expectable that the still higher rate of expansion is gathered.

[0015]

[Effect of the Invention] The point of the following which was a problem has been improved with equipment conventional by having done in this way.

[0016] Since there is no joint in a silicon belt, it is hard to go out, and the rate of expansion came (finishing [a check of the expansion beyond twice of 110% i.e., original die length,]) to be gathered.

[0017] Since the silicon belt is not pressed down, even if it extends, there is no strain of a spool mold, the expansion direction and the rate of expansion are the same, and analysis becomes easy to carry out it in every location on (6) and a belt [drawing 2].

[0018] A silicon belt can create the thing of free magnitude now at a cheap price by

changing a template, and sterilization and wearing to equipment also became easy.

[0019] By the conventional approach, although microscope observation in the condition of having extended the cell was impossible, it became observable [the cell in the condition (8) that the rate of expansion of arbitration extended by inserting the glass plate (7) of various die length into a silicon belt] [drawing 3].

[0020] Since it was a motor with a precision a high torque stepping motor is strong as the name suggests, and high usually used for positioning of the print head of a printer etc., about the rate of expansion, it is a fine step and a setup became broadly possible. Since the silicon belt was furthermore extended directly, precision was high, and room for deviation to come out was lost.

[0021] A motion of a stepping motor can be easily programmed using a controller, and rate of expansion, flexible acceleration, expansion time amount and halt / flexible frequency etc. can change it now easily. [-- round-head one day -- applying -- a cell -- expansion] -- it carried out and what [a flexible stimulus is further given also for after carrying out fixed time amount expansion] came be made for the first time by using this invention.

[0022] It can be operational only with the program of a controller, without touching hardware, and a motion of a stepping motor can also make now a change of the program in the middle of flexible, without touching parts [finishing / sterilization].

[0023] Where a silicon belt is extended, a cell is cultivated, and the effect contraction of a basal plane affects a cell can also be observed now by returning it to the original condition.

[0024] The fragment (the shape of a ring) of a blood vessel is connected with a direct device, and it can experiment now in it.

[0025] The expansion device using a silicon belt is very simple, simplification in the field of equipments was attained compared with [the conventional approach 2] (downsizing), and 1/10 or less was the amount of money of a system.

[Translation done.]

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TECHNICAL FIELD

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PRIOR ART

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EFFECT OF THE INVENTION

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MEANS

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EXAMPLE

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DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]

[Drawing 1] It is the perspective view of the device of this invention.

[Drawing 2] A It is the top view of the silicon belt before telescopic motion.

B It is the top view of the silicon belt after telescopic motion.

[Drawing 3] It is the perspective view which it is at the expansion time and is fixing the silicon belt.

[Drawing 4] On the other hand, it is the top view of the flexible device of tropism.

C It is a top view before telescopic motion.

D It is a top view after telescopic motion.

[Drawing 5] It is the perspective view of the flexible device of radiation directivity.

E It is a perspective view before telescopic motion.

F It is a perspective view after telescopic motion.

[Description of Notations]

1 Silicon Belt

2 Rod

3 Arm

4 Leading Screw

5 Silicon Belt before Expansion

6 Silicon Belt after Expansion

7 Glass Plate

8 Silicon Belt Fixed in the Condition of Having Extended

9 Silicon Film before Expansion

10 Silicon Film after Expansion

11 Clip

12 Cam

13 Silicon Membranous Bottom before Expansion

14 Silicon Membranous Bottom after Expansion

15 Petri Dish (Side Face)

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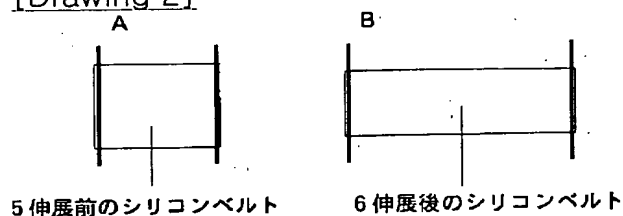
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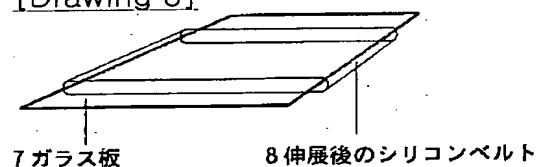
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DRAWINGS

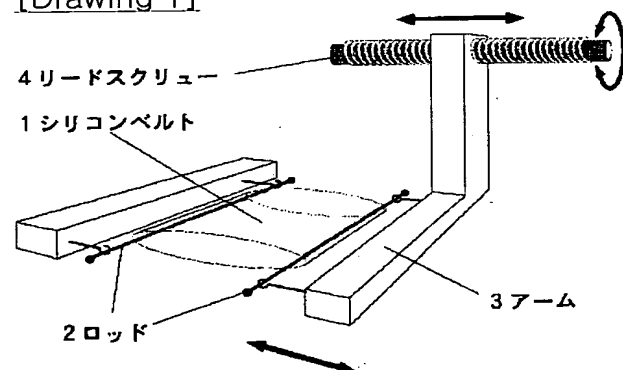
[Drawing 2]



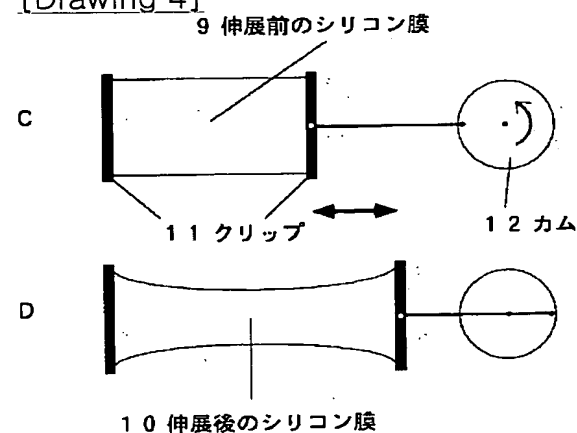
[Drawing 3]



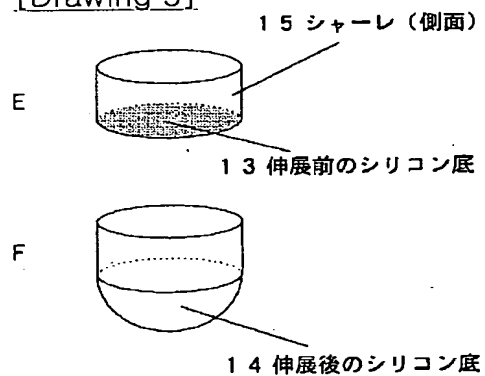
[Drawing 1]



[Drawing 4]



[Drawing 5]



[Translation done.]

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(11) 特許出願公開番号

特開平10-155475

(43) 公開日 平成10年(1998) 6月16日

(51) Int.Cl.⁶

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識別記号

F I

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A

審査請求 未請求 請求項の数 3 書面 (全 4 頁)

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(22) 出願日 平成8年(1996)12月2日

特許法第30条第1項適用申請有り 平成8年10月25日
日本細胞生物学会開催の「日本細胞生物学会第49回大会」において文書をもって発表

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(72) 発明者 市川 正雄

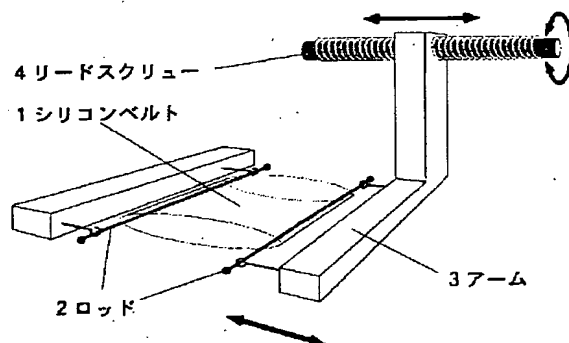
東京都千代田区神田美土代町7番地 日本
サーボ株式会社内

(54) 【発明の名称】 シリコンベルトを使った培養細胞用伸縮刺激負荷装置

(57) 【要約】

【課題】 従来の培養細胞伸縮装置は、細胞を伸展した際にひずみを生じ、場所により変形の具合が異なっていて解析がしにくかった。また引き伸ばす機構が複雑なため滅菌や装着に手間がかかった。

【解決手段】 本発明はこのような課題を解決するために、表面上に細胞を培養したシリコンベルト(1)に2本のロッド(2)を挿入し、そのロッドをアーム(3)に引っ掛け、高トルクステッピングモーターの時計回り・反時計回りの回転運動はリードスクリュー(4)を使ってアームのピストン運動に変換し、アームを左右に振ることでシリコンベルトを伸縮させるようにした。



【特許請求の範囲】

【請求項1】 担体にベルト状のシリコン膜（1）を使った培養細胞用伸縮刺激負荷装置

【請求項2】 動力にステッピングモーターを使い、その回転運動をリードスクリュー（4）で直線運動に変えた請求項1記載の培養細胞用伸縮刺激負荷装置

【請求項3】 動力にステッピングモーターを使い、その回転運動をタイミングベルトで直線運動に変えた請求項1記載の培養細胞用伸縮刺激負荷装置

【発明の詳細な説明】

【0001】

【発明の属する技術分野】この発明は、培養細胞や組織に伸縮刺激や伸展刺激を与える技術に関するものである。

【0002】

【従来の技術】一般に、培養細胞などに伸縮刺激を与えるには細胞外マトリックスなどをコーティングしたシリコン膜上に細胞を培養し、それをシリコン膜ごと伸縮させる方法が採られている。従来シリコン膜を伸展させる装置としては、伸展の方向性から考えて一方向性のもの【図4】と、放射状のもの【図5】が使われてきた。

【0003】一方向性のものは長方形のシリコン膜（9）の両端をクリップ（11）を使ってきつく固定し、それをカム（12）を使ったシンクロナスモーターの回転運動をピストン運動に変える機構により引き伸ばしたり（10）、元の長さに戻したり（9）する方法

【従来の方法1】が使われている【図4】。

【0004】放射状のものは底面（13）だけがシリコン膜でできているシャーレ（15）を、下から吸引することで底のシリコン膜を引き伸ばしたり（14）元の状態に戻したり（13）する方法【従来の方法2】が使われている（米国フレックスセル社：特許番号4789601、4822741、4839280）【図5】。

【0005】

【発明が解決しようとする課題】

【従来の方法1】について シリコン膜（9）の両端は引き伸ばしても離れないようにクリップ（11）できつく固定されているため、引き伸ばした際には（10）のような糸巻き状のひずみを生じ、場所によって変形の具合が異なるため伸展方向の解析をしにくくしていた。そしてクリップなどの固定器具を含む機材には滅菌操作が必要であったが、繰り返し高温・高圧・高湿度のオートクレーブ滅菌などに耐え、かつ加工などもやりやすい材質のパネやネジは少なく、さらに実験のたびの固定操作は煩雑であった。またシンクロナスモーターとカムを使ったデバイスは振幅の変更もハードウェア自身を組み替えずにはならないため面倒で、かつ【周期的に一時停止を含む伸縮運動】の設定や伸縮加速度の変更は不可能であった。

【0006】【従来の方法2】について 引き伸ばされ

たシリコン膜（14）には放射状に張力がかかるため、場所により張力方向が異なり伸展方向の解析をしにくくしていた。また伸展されているのはシリコン膜の周辺部のみで中央部はほとんど引き伸ばされないことも指摘されていた。さらに周辺部においても伸展率は構造的に24%までしか得られないという制限もあった。そして吸引という間接的な方法でシリコンを引き伸ばしているの、バックリングの磨耗やゴミの付着などにより、設定した伸展率に比べて実際の伸展率に狂いが出る可能性があった。また既製のシリコンシャーレは大きさが決まっているため自由度が少なく、かつ高価であった。さらに吸引ユニット（含コンピューター、吸引ポンプ）も大がかりなもので場所をとり、かつ高価であった。

【0007】

【課題を解決するための手段】本発明はこのような課題を解決するために担体のシリコン膜をベルト状にしたもの（1）を用い、それを高トルクステッピングモーターとリードスクリューを使って伸縮させるものである【図1】。細胞などが付着しているシリコンベルト（1）の内側に二本のロッド（2）を挿入し、そのロッドをそれぞれ左右のアーム（3）に引っかける。高トルクステッピングモーターの時計回り・反時計回りの回転運動はリードスクリュー（4）を使ってアームのピストン運動に変換する。アームを左右に振ることでシリコンベルトを伸縮させることができる。

【0008】

【実施例】シリコンベルトはダウコーニングアジア社のシルボット184W/Cを用い、ガラスの試験管、もしくはシリコン棒をテンプレートにしてディッピング法で皮膜を作り、熱をかけて硬化させる。剥ぎ取った袋状のシリコンを輪切りにすればシリコンベルトができる。

【0009】シリコンベルトはオートクレーブ滅菌、ロッドとアームは乾熱滅菌をそれぞれ独立に行うが、無菌的に組み立てるのも簡単である。

【0010】高トルクステッピングモーターの回転運動はカーク社のリードスクリューを使って直線運動に変換した。

【0011】高トルクステッピングモーターの回転運動はタイミングベルトを使って直線運動に変換する事も可能である。

【0012】日本サーボ株式会社のステッピングモーターの動きは、同社のインテリジェントコントロールドライバを使って制御することで、0%から少なくとも110%の範囲で0.1%刻みの高い精度で伸展率が設定可能となり、伸縮加速度・伸展時間・一時停止・伸縮頻度などの変換を含むプログラムの変更も滅菌済みのハードウェアを組み替えることなく容易に設定できた。

【0013】アームのロッドを引っかける部分は滅菌の必要があるため、リードスクリューにつながる可動部分からネジなどを使って脱着可能にした方が便利である。

【0014】顕微鏡観察の必要のない場合にはラテックスシリコンの代わりにラテックスゴムを用いればさらに高い伸展率が上げられることが期待できる。

【0015】

【発明の効果】このようにしたことて従来の装置では問題であった以下の点が改善された。

【0016】シリコンベルトには継ぎ目がないから切れにくく、伸展率が上げられるようになった（110%、即ちオリジナルの長さの倍以上の伸展を確認済み）。

【0017】シリコンベルトは押さえていないから伸展しても糸巻き型のひずみはなく（6）、ベルト上のどの位置でも伸展方向・伸展率は同じで解析がしやすくなった【図2】。

【0018】シリコンベルトはテンプレートを変えることで自由な大きさのものを安い値段で作成できるようになり、滅菌や装置への装着も簡単になった。

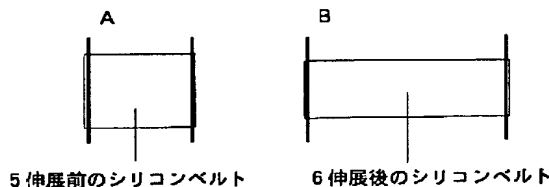
【0019】細胞を引き伸ばした状態での顕微鏡観察は従来の方法では不可能であったが、シリコンベルトの中にいろいろな長さのガラス板（7）を挿入することで任意の伸展率で引き伸ばした状態（8）の細胞も観察可能となった【図3】。

【0020】高トルクステッピングモーターはその名の通り力が強く、また通常プリンターの印字ヘッドの位置決めなどに使われている精度の高いモーターなので、伸展率を細かいステップでかつ広範囲に設定可能になった。さらにシリコンベルトを直接引き伸ばしているので精度は高く、狂いが出る余地はなくなった。

【0021】ステッピングモーターの動きはコントローラを使って簡単にプログラムでき、伸展率・伸縮加速度・伸展時間・一時停止・伸縮頻度などが簡単に変更できるようになった。【丸一日かけて細胞を伸展】させたり、【一定時間伸展させた後にさらに伸縮刺激を与える】ことも本発明を使うことで初めてできるようになった。

【0022】ステッピングモーターの動きはハードウェアを触ることなしにコントローラのプログラムのみで操作可能であり、伸縮途中のプログラムの変更でも滅菌済みのパーツを触らずに行えるようになった。 *

【図2】



* 【0023】シリコンベルトを伸展した状態で細胞を培養し、それを元の状態に戻すことで、基底面の収縮が細胞に及ぼす影響も観察できるようになった。

【0024】血管の断片（リング状）を直接デバイスにつないで実験できるようになった。

【0025】シリコンベルトを使った伸展機構はとても単純であり、【従来の方法2】と比べると機材の面での簡素化が図られ（ダウンサイジング）、システムの金額は10分の1以下になった。

10 【図面の簡単な説明】

【図1】本発明のデバイスの斜視図である。

【図2】A 伸縮前のシリコンベルトの平面図である。

B 伸縮後のシリコンベルトの平面図である。

【図3】伸展時点でシリコンベルトを固定している斜視図である。

【図4】一方向性の伸縮デバイスの平面図である。

C 伸縮前の平面図である。

D 伸縮後の平面図である。

【図5】放射方向性の伸縮デバイスの斜視図である。

20 E 伸縮前の斜視図である。

F 伸縮後の斜視図である。

【符号の説明】

1 シリコンベルト

2 ロッド

3 アーム

4 リードスクリュー

5 伸展前のシリコンベルト

6 伸展後のシリコンベルト

7 ガラス板

30 8 伸展した状態で固定されたシリコンベルト

9 伸展前のシリコン膜

10 伸展後のシリコン膜

11 クリップ

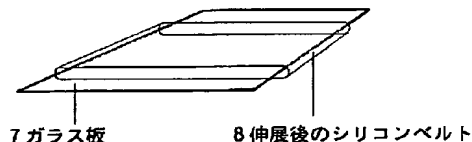
12 カム

13 伸展前のシリコン膜性の底

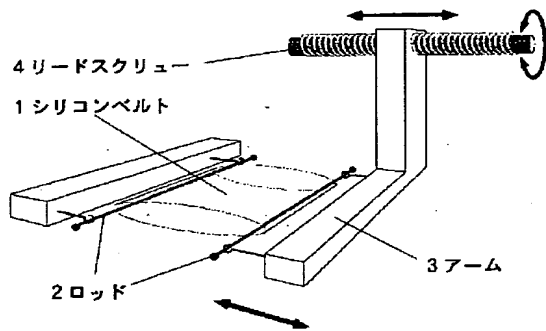
14 伸展後のシリコン膜性の底

15 シャーレ（側面）

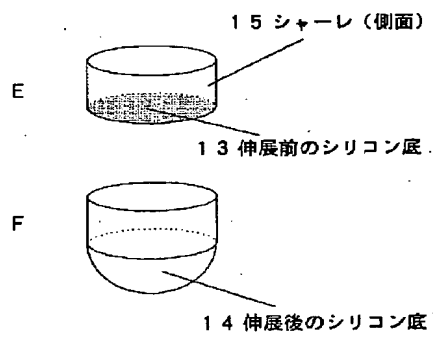
【図3】



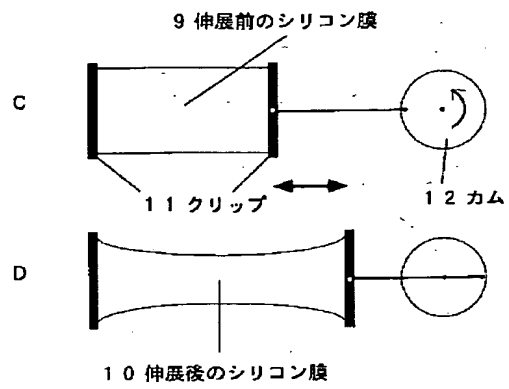
【図1】



【図5】



【図4】



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